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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/761,557	01/21/2004	D. James Surmeier	Nwestern-08739	2838

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Casimir Jones, S.C.
440 Science Drive
Suite 203
Madison, WI 53711

EXAMINER	
CHONG, KIMBERLY	

ART UNIT	PAPER NUMBER
1635	

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02/06/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/761,557	SURMEIER ET AL.	
	Examiner	Art Unit	
	Kimberly Chong	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-21 and 23-25* is/are rejected.

7)☒ Claim(s) *22,23* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/31/2007 has been entered.

Status of Application/Amendment/Claims

Applicant's response filed 10/31/2007 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 10/04/2007 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed on 10/31/2007, claims 18-25 are pending in the application.

New Claim Objections and Rejections

Claim Objections

Claims 22 and 23 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims and deleting non-elected subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 18-21 and 24-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Erisir et al. (J. Neurophysiology. 1999, Vol. 82: 2476-2489 cited on Applicant's IDS filed 11/23/2005), Baranauskas et al. (Journal of Neuroscience 1999, Vol. 10(15): 6394-6404 cited on Applicant's IDS filed 11/23/2005), Tkatch et al. (Society for Neuroscience, 1999, Vol. 25L Abstract 179.17), Weiser et al. (cited on Applicant's IDS filed 11/23/2005),Tuschl et al. (cited on PTO form 892 field 03/09/2007) and Low et al. (cited on PTO form 892 field 03/09/2007).

Claims 18-21 and 24-25 are drawn to a method of manipulating neuronal ion channels comprising transfecting a fast spiking neuronal cell with a vector encoding a siRNA targeted to Kv3.4, wherein said cell comprises a co-assembled complex of

mammalian Kv3.1, Kv3.2, Kv3.3 and Kv3.4 and wherein said siRNA is capable of inhibiting expression of Kv3.4 which results in a decrease in said sustained high frequency discharge in said cell, wherein the frequency is greater than 100 or 150 Hz, wherein the mammalian Kv3.4 is rat or human and further comprising the step of transplanting said cell into a subject.

Baranauskas et al. teach Kv3.1 and Kv3.2 are both detected in globus pallidus (GP) fast spiking neurons and teach expression from such genes in potassium currents is associated with the capacity to discharge at high rates for sustained periods of time in neurons (see page 6401, particularly column 1 and page 6402, particularly last paragraph column 2). Baranauskas et al. teach this high frequency discharge of Kv3.1 and Kv3.2 is found in rats and primates (see page 6402, particularly last paragraph column 2) and teach aberrant high frequency discharge is thought to be critical in the emergence of Parkinson's disease (see page 6403). Baranauskas et al. teach genetic manipulation that normalizes the ratio of potassium channels in cells would assist in suppressing unwanted high frequency activity from said channels (see page 6403).

Erisir et al. teach Kv3.1 and Kv3.2 are predominantly expressed in fast spiking neuronal cells and teach expression from said genes is needed to facilitate the sustained high-frequency firing in potassium channels (see page 2476-2477). Erisir et al. teach the fast spiking neurons have a firing frequency of greater than 150 Hz (see Figure 2). Erisir et al. teach that blocking the expression of Kv3.1 and Kv3.2 leads to a decreased frequency of firing in fast spiking neurons (see Figure 9 and pages 2485-2487).

Neither Erisir et al. nor Baranauskas et al. teach manipulating Kv3.4 nor teach inhibiting expression of Kv3.4 using a siRNA compound.

Tkatch et al. teach potassium Kv3.4 channels are associated with spike broadening during burst firing in GP neurons and teach this bursting is increased in Parkinson's disease (see abstract). Tkatch et al. further genes Kv3.1, Kv3.2, Kv3.3 and Kv3.4 were detected together in GP neurons (see abstract).

Weiser et al. describe cloning of Kv3.1, Kv3.2, Kv3.3 and Kv3.4 into cells and teach expression of all four related potassium channels in brain tissue (see page 952, pages 956-957 and Figure 958).

Tuschl et al. teach siRNA molecules which are capable of mediating target-specific RNA interference and teach such siRNA molecules have improved safety and efficacy compared to therapeutic equivalents (see page 3, lines 12-16). Tuschl et al. teach siRNA can be expressed in a vector (see page 7, lines 17-23). Tuschl et al. teach a method of siRNA preparation from gene sequences (see page 38). Tuschl et al. teach such siRNA molecules can be used for determining the function of a gene in a cell by modulating the expression of said gene (see page 8, lines 11-13).

Low et al. teach a method of transfecting oligonucleotide compounds into cells *ex vivo* using an expression vector and teach transplanting said cells into a subject to be used as a vaccine to inhibit gene expression (see column 4, lines 6-60).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to target the Kv3.4 gene (as taught by Tkatch et al.) and it would have been obvious to one of skill in the art to modulate the expression of Kv3.4 using

siRNA (as taught by Tuschl) for the purpose of determining the function of said gene in fast spiking neurons and the role this gene expression plays in Parkinson's disease. Further it would have been obvious for one of ordinary skill in the art to transfect siRNA into cells and transplant said cells into a subject to be used as a vaccine to inhibit gene expression, as taught by Low et al.

One would have been motivated to modulate the expression of a Kv3.4 gene because Baranauskas et al. teach related potassium channels Kv3.1 and Kv3.2 are capable of sustained high frequency discharge in GP neuronal cells which have been indicated in Parkinson's disease and Tkatch et al. teach that Kv3.4, like Kv3.1 and Kv3.2, are responsible for increased burst firing in GP cells. Given that Baranauskas et al. teach the symptoms of Parkinson's disease are thought to result from an increased bursting activity in GP neurons and given Tkatch et al. recognized Kv3.4 was responsible for increased burst firing in GP cells and also recognized that this increased frequency of discharge is increased in Parkinson's disease, one of skill would have been motivated to manipulate the expression of Kv3.4 to decrease the high frequency discharge from the potassium channel to further study the role Kv3.4 has in the emergence of Parkinson's disease in humans. One of skill in the art would have wanted to use the most efficient method of inhibiting gene expression from a gene and therefore would have been motivated to generate a siRNA targeted to a Kv3.4 gene as taught by Tuschl et al. and Weiser et al. One would have clearly used a siRNA particularly given that Tuschl et al. teach determining or modulating, particularly inhibiting the function of a such a gene, provide valuable information and therapeutic benefits in the field of

medicine (see page 8, lines 25- 28). Moreover, one would have been motivated to transfect cells ex vivo using a siRNA because Low et al. teach transfected cells can be efficiently transplanted into a subject and work to inhibit gene expression

Finally, one would have a reasonable expectation of success at targeting a Kv3.4 gene given Weiser et al. teach the cDNA to said gene and Tuschl et al. teach the basic blue print of making and using siRNA to silence gene expression from any target gene of interest. Further, Low et al. teach efficient transplantation of cells transfected with an antisense oligonucleotide and one would expect the same success using a siRNA since each molecule is a nucleic acid capable of inhibiting gene expression.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Response to Applicant's Arguments

Re: Claim Rejections - 35 USC § 112

The rejection of claims 4 and 10 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is moot in view of the canceled claims filed in the amendment of 11/30/2007.

Re: Claim Rejections - 35 USC § 103

The rejection of claims 4 and 10 under 35 U.S.C. 103(a) as being unpatentable over Retting et al. (cited on Applicant's IDS filed 11/23/2005), Low et al. (cited on PTO

form 892 field 03/09/2007), Tuschl et al. (cited on PTO form 892 field 03/09/2007) and evidenced by Weiser et al. (cited on Applicant's IDS filed 11/23/2005) is moot in view of the canceled claims filed in the amendment of 11/30/2007.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Kimberly Chong/
Examiner
Art Unit 1635